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=> file medline caplus embase biosis cancerlit
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=> s trimer?
L1 53714 TRIMER?

=> s mutant? or mutein? or variant? or wild?
L2 1609354 MUTANT? OR MUTEIN? OR
VARIANT? OR WILD?

=> s dominant-negative or dominant (w) negative
L3 46867 DOMINANT-NEGATIVE OR DOMINANT
(W) NEGATIVE

=> s l2 (s) l3
L4 23245 L2 (S) L3

=> s l4 (s) l1
L5 52 L4 (S) L1

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L6 ANSWER 1 OF 31 EMBASE COPYRIGHT 2003
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on STN
ACCESSION NUMBER: 2003362578 EMBASE
TITLE: Interactions of FliJ with the Salmonella
type III flagellar

export apparatus.

AUTHOR: Fraser G.M.; Gonzalez-Pedrajo B.;
Tame J.R.H.; Macnab R.M.
CORPORATE SOURCE: R.M. Macnab, Dept. Molec.
Biophys./Biochem. 0734, Yale

University, 266 Whitney Ave., New Haven,
CT 06520-8114,

United States. robert.macnab@yale.edu

SOURCE: Journal of Bacteriology, (2003)
185/18 (5546-5554).

Refs: 22

ISSN: 0021-9193 CODEN: JOBAAY

COUNTRY: United States

DOCUMENT TYPE: Journal; Article

FILE SEGMENT: 004 Microbiology

LANGUAGE: English

SUMMARY LANGUAGE: English

AB FliJ, a 17-kDa protein, is a soluble component of
the Salmonella type III

flagellar protein export system that has

antiaggregation properties and

several other characteristics that suggest it may

have a chaperone-like

function. We have now examined this protein in

detail. Ten-amino-acid

scanning deletions covering the entire 147-amino-

acid sequence were tested

for complementation of a fliJ null strain; only the first
and last

deletions complemented. A few of the deletions,

especially towards the C

terminus, exerted a ***dominant*** ***negative***
effect on

wild -type cells, indicating that they were
actively interfering

with function. Two truncated versions of FliJ,

representing its N- and

C-terminal halves, failed to complement and were

not dominant. We tested

for FliJ self-association by several techniques. Size-

exclusion

chromatography (Superdex 200) indicated an

apparent molecular mass of

around 50 kDa, which could reflect either

multimerization or an elongated

shape or both. Multiangle light scattering gave a

peak value of 20 kDa,

close to the molecular mass of the monomer.

Analytical ultracentrifugation

gave evidence for weak self-association as a

trimer or tetramer.

It was known from previous studies that FliJ

interacts with the N-terminal

region of FliH, a negative regulator of the ATPase

FliI. Using both

truncation and deletion versions of FliJ, we now

show that it is its

C-terminal region that is responsible for this

interaction. We also show

that FliJ interacts with the soluble cytoplasmic

domain of the largest

membrane component of the export apparatus,

FliA; although small deletions

in FliJ did not interfere with the association, both

truncated versions

failed to associate, indicating that a substantial

amount of the central

region of the FljJ sequence participates in the association. We present a model summarizing these multiple interactions.

L6 ANSWER 2 OF 31 EMBASE COPYRIGHT 2003 ELSEVIER INC. ALL RIGHTS RESERVED.

on STN DUPLICATE 1
ACCESSION NUMBER: 2002309005 EMBASE
TITLE: Collagen X chains harboring Schmid metaphyseal

chondrodysplasia NC1 domain mutations are selectively retained and degraded in stably transfected cells.

AUTHOR: Wilson R.; Freddi S.; Bateman J.F.
CORPORATE SOURCE: J.F. Bateman, Murdoch Childrens Research Institute, Royal Children's Hospital, Parkville, Vic. 3052, Australia.

bateman@cryptic.rch.unimelb.edu.au
SOURCE: Journal of Biological Chemistry, (12 Apr 2002) 277/15

(12516-12524).

Refs: 35

ISSN: 0021-9258 CODEN: JBCHA3

COUNTRY: United States

DOCUMENT TYPE: Journal; Article

FILE SEGMENT: 022 Human Genetics

029 Clinical Biochemistry

033 Orthopedic Surgery

LANGUAGE: English

SUMMARY LANGUAGE: English

AB Collagen X is a short chain, homotrimeric collagen expressed specifically

by hypertrophic chondrocytes during endochondral bone formation and growth. Although the exact role of collagen X remains unresolved, mutations in the COL10A1 gene disrupt growth plate function and result in Schmid metaphyseal chondrodysplasia (SMCD).

With the exception of two mutations that impair signal peptide cleavage during .alpha.1(X) chain biosynthesis, SMCD mutations are clustered within the carboxyl-terminal

NC1 domain. The formation of stable NC1 domain ***trimers*** is a

critical stage in collagen X assembly, suggesting that mutations within this domain may result in subunit mis-folding or reduce ***trimer***

stability. When expressed in transiently transfected cells, .alpha.1(X)

chains containing SMCD mutations were unstable and presumed to be degraded

intracellularly. More recently, in vitro studies have shown that certain

missense mutations may exert a ***dominant*** ***negative***

effect on .alpha.1(X) chain assembly by formation of ***mutant***

homotrimers and normal- ***mutant***

heterotrimers. In contrast, analysis of cartilage tissue from two SMCD patients revealed that the

truncated ***mutant*** message was fully

degraded, resulting in 50% reduction of functional collagen X within the growth plate. Therefore, in

the absence of data that conclusively demonstrates the full cellular

response to ***mutant*** collagen X chains, the molecular mechanisms

underlying SMCD remain controversial. To address this, we closely examined

the effect of two NC1 domain mutations, one frameshift mutation

(1963del10) and one missense mutation (Y598D), using both

semipermeabilized cell and stable cell transfection expression systems.

Although able to assemble to a limited extent in both systems, we show

that, in intact cells, collagen X chains harboring both SMCD mutations did

not evade quality control mechanisms within the secretory pathway and were

degraded intracellularly. Furthermore, co-expression of ***wild***

-type and ***mutant*** chains in stable transfected cells demonstrated

that, although ***wild*** -type chains were secreted, ***mutant***

chains were largely excluded from hetero-***trimer*** formation. Our

data indicate, therefore, that the predominant effect of the NC1 mutations

Y598D and 1963del10 is a reduction in the amount of functional collagen X

within the growth cartilage extracellular matrix.

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on STN DUPLICATE 2
ACCESSION NUMBER: 2001045457 EMBASE

TITLE: CD154 variant lacking tumor necrosis factor homologous

domain inhibits cell surface expression of wild-type

protein.

AUTHOR: Su L.; Garber E.A.; Hsu Y.-M.

CORPORATE SOURCE: Y.-M. Hsu, Dept. of Protein Engineering, Biogen, Inc., 12

Cambridge Center, Cambridge, MA 02142, United States.

yen-ming_hsu@biogen.com

SOURCE: Journal of Biological Chemistry, (19 Jan 2001) 276/3

(1673-1676).

Refs: 17

ISSN: 0021-9258 CODEN: JBCHA3

COUNTRY: United States

DOCUMENT TYPE: Journal; Article

FILE SEGMENT: 029 Clinical Biochemistry

LANGUAGE: English

SUMMARY LANGUAGE: English

AB X-linked hyper-IgM (XHIM) syndrome is an immunological disorder resulting

from mutations in the CD154 gene. Some mutations occur in splicing sites

and result in transcripts encoding ***wild*** -type and ***mutant***

proteins. These ***mutants*** lack the tumor necrosis factor

homologous (TNFH) domain and consequently fail to ***trimerize***

Given that the TNFH domain is responsible for ***trimerization***, one

may predict that the TNFH ***mutant*** can not participate in the assembly of ***wild*** -type CD154. Thus, it was puzzling why these patients exhibit XHIM pheno-type, presumably resulting from a lack of functional CD154. One possibility is that the TNFH ***mutant*** exhibits a ***dominant*** ***negative*** effect over the ***wild*** -type protein. To investigate this, we coexpressed the ***wild*** -type protein and a TNFH ***mutant*** and examined the biochemical and functional properties of the resulting CD154 products. We demonstrate that despite the lack of the TNFH domain, the TNFH ***mutant*** can associate with the ***wild*** -type protein. Furthermore, such an association compromises the ability of the ***wild*** -type protein to mature onto the cell surface. These results provide a mechanism for the defect of CD154 in XHIM patients producing both ***wild*** -type and TNFH ***variants*** and suggest that besides the TNFH domain, the stalk region participates in the assembly of CD154 ***trimers***.

L6 ANSWER 4 OF 31 MEDLINE on STN
 DUPLICATE 3
 ACCESSION NUMBER: 2001267781 MEDLINE
 DOCUMENT NUMBER: 21257784 PubMed ID:
 11358428

TITLE: Coexpression of normal and mutated
 CD40 ligand with
 deletion of a putative RNA lariat
 branchpoint sequence in
 X-linked hyper-IgM syndrome.

AUTHOR: Zhu X; Chung I; O'Gorman M R;
 Scholl P R

CORPORATE SOURCE: Disease Pathogenesis
 Program, Children's Memorial Institute
 for Education and Research, Chicago,
 Illinois 60614, USA.

SOURCE: CLINICAL IMMUNOLOGY, (2001
 Jun) 99 (3) 334-9.

Journal code: 100883537. ISSN: 1521-
 6616.

PUB. COUNTRY: United States
 DOCUMENT TYPE: Journal; Article; (JOURNAL
 ARTICLE)

LANGUAGE: English
 FILE SEGMENT: Priority Journals
 ENTRY MONTH: 200106

ENTRY DATE: Entered STN: 20010625
 Last Updated on STN: 20010625
 Entered Medline: 20010621

AB We describe a novel CD40 ligand (CD40L) splicing
 mutation in a patient
 with X-linked hyper-IgM syndrome (X-HIM)
 associated with alternate
 splicing of exon 3, resulting in the expression of both
 full-length and
 exon-3-skipped CD40L mRNA. The mutation is an
 8-bp deletion 25 bp

upstream of the intron 2/exon 3 junction which
 overlaps a putative RNA
 branchpoint, suggesting that it may impair RNA lariat
 formation. The
 exon-3-skipped CD40L transcript encodes a
 truncated protein (CD40LDeltaE3)
 encompassing the cytoplasmic, transmembrane,
 and extracellular stalk
 domains, but lacking the CD40L receptor binding
 domain. CD40LDeltaE3
 protein expression was readily detectable in
 transfected Cos cells by
 immunofluorescence. In cells cotransfected with
 CD40LDeltaE3 and
 wild -type CD40L, expression of
 CD40LDeltaE3 did not inhibit the
 expression of ***wild*** -type CD40L monomers,
 but strongly inhibited
 staining by the conformationally sensitive anti-
 CD40L mAb 5c8, suggesting
 that CD40LDeltaE3 acts in a ***dominant***
 negative manner
 to inhibit the assembly of functional CD40L
 trimers. This
 mechanism may contribute to the pathophysiology of
 CD40L deficiency in
 X-HIM patients with leaky splice site mutations.
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on STN DUPLICATE 4
 ACCESSION NUMBER: 2001118615 EMBASE
 TITLE: Alternative activation of extracellular
 signal-regulated

protein kinases in curcumin and arsenite-
 induced HSP70 gene
 expression in human colorectal carcinoma
 cells.

AUTHOR: Chen Y.-C.; Tsai S.-H.; Shen S.-C.;
 Lin J.-K.; Lee W.-R.

CORPORATE SOURCE: Prof. Y.-C. Chen, Graduate
 Institute of Pharmacognosy,
 Taipei Medical College, 250 Wu-Hsing St.,
 Taipei,

Taiwan, Province of China.

yc3270@tmc.edu.tw

SOURCE: European Journal of Cell Biology,
 (2001) 80/3 (213-221).

Refs: 52
 ISSN: 0171-9335 CODEN: EJCBND

COUNTRY: Germany
 DOCUMENT TYPE: Journal; Article
 FILE SEGMENT: 016 Cancer
 022 Human Genetics
 029 Clinical Biochemistry
 048 Gastroenterology

LANGUAGE: English

SUMMARY LANGUAGE: English
 AB We have investigated the regulation mechanism of
 chemical stress-induced
 HSP70 gene expression in human colorectal
 carcinoma cells (COLO205 and
 HT29). Our data show that chemical treatments
 including sodium arsenite
 and curcumin, induced significant synthesis of
 HSP70 and its mRNA. The
 induced HSP70 gene expression appears to be
 increased at the

transcriptional level. The increase in HSP70 gene expression by both chemicals is associated with an increase in HSF binding to HSE and induction of HSF1 di- or ***trimerization***. Phosphorylation and activation of extracellular signal-regulated proteins (ERK1/2) were detected in sodium arsenite-treated COLO205 and HT29 cells, and the free radical scavenger N-acetyl-L-cysteine (NAC) was able to inhibit this ERK1/2 activation and HSP70 gene expression. MAPK blockade by the specific MEK1 inhibitor (PD98059) decreased the ability of sodium arsenite to increase HSP70 gene expression in a dose-dependent manner along with dephosphorylation of ERK1/2 proteins. In contrast to arsenite treatment, activation of ERK1/2 was not detected in curcumin-treated colorectal carcinoma cells, and NAC and PD98059 did not show any inhibitory effect on HSP70 gene expression induced by curcumin. Overexpression of a ***dominant*** ***negative*** ***mutant*** of mitogen-activated protein kinase kinase kinase 1 (MEKK1-DN) prevents arsenite-induced ERK1/2 phosphorylation and HSP70 protein synthesis. These results indicated that the ERK signaling pathway can participate in HSP70 gene expression induced by the prooxidant sodium arsenite, but not by the antioxidant curcumin.

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on STN DUPLICATE 5
ACCESSION NUMBER: 2001258772 EMBASE
TITLE: Association of phosphatidylinositol 3-kinase composed of p110.beta.-catalytic and p85-regulatory subunits with the small GTPase Rab5.

AUTHOR: Kurosu H.; Katada T.
CORPORATE SOURCE: T. Katada, Dept. of Physiological Chemistry, Grad. Sch. of Pharmaceut. Sciences, University of Tokyo, 7-3-1 Hongo, Bunkyo-ku, Tokyo 113-0033, Japan.
katada@mol.f.u-tokyo.ac.jp

SOURCE: Journal of Biochemistry, (2001) 130/1 (73-78).

Refs: 31

ISSN: 0021-924X CODEN: JOBIAO

COUNTRY: Japan

DOCUMENT TYPE: Journal; Article

FILE SEGMENT: 029 Clinical Biochemistry

LANGUAGE: English

SUMMARY LANGUAGE: English

AB A family of phosphatidylinositol 3-kinases (PI 3-kinase), comprising three major classes (I-III) in terms of substrate specificity and regulation, play important roles in a variety of cell functions. We previously

reported that the class-I heterodimeric PI 3-kinase consisting of p110.beta.-catalytic and p85-regulatory subunits is synergistically activated by two different types of membrane receptors, one possessing tyrosine kinase activity and the other activating ***trimeric*** G proteins. Here we report an additional unique feature of the p110.beta./p85 PI 3-kinase. The small GTPase Rab5 was identified as a binding protein for the p110.beta.-catalytic subunit in a yeast two-hybrid screening system. The interaction appears to require at least two separated amino-acid sequences present specifically in the .beta. isoform of p110 and the GTP-bound form of Rab5. The expressions of constitutively active and ***dominant*** ***negative*** ***mutants*** of Rab5 in THP-1 cells induce the stimulation and inhibition, respectively, of protein kinase B activity, which is dependent on the PI 3-kinase product phosphatidylinositol 3,4,5-triphosphate. These results suggest that there is a specific interaction between GTP-bound Rab5 and the p110.beta./p85 PI 3-kinase, leading to efficient coupling of the lipid kinase product to its downstream target, protein kinase B.

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on STN DUPLICATE 6
ACCESSION NUMBER: 2001259607 EMBASE
TITLE: Analysis of dominant-negative effects of mutant Env

proteins of human immunodeficiency virus type 1.

AUTHOR: Iwatani Y.; Kawano K.; Ueno T.; Tanaka M.; Ishimoto A.; Ito M.; Sakai H.

CORPORATE SOURCE: H. Sakai, Department of Viral Oncology, Institute for Virus Research, Kyoto University, Sakyo-Ku, Kyoto 606-8507,

Japan. hsakai@virus.Kyoto-u.ac.jp
SOURCE: Virology, (20 Jul 2001) 286/1 (45-53).

Refs: 44

ISSN: 0042-6822 CODEN: VIRLAX

COUNTRY: United States

DOCUMENT TYPE: Journal; Article

FILE SEGMENT: 004 Microbiology

LANGUAGE: English

SUMMARY LANGUAGE: English

AB The Env protein of human immunodeficiency virus type 1 is assembled into a stable ***trimer***, and oligomerization is required for maintenance of viral infectivity. This property of Env suggests that Env

mutants may have a ***dominant*** - ***negative*** effect on virus infectivity. To investigate this possibility, we established a packaging cell line in which both ***wild*** -type and ***mutant***

Env proteins could be expressed simultaneously in a single cell. We analyzed the effects of two types of Env ***mutants*** : cytoplasmic tail-truncated TM ***mutants*** and a ***mutant*** defective in gp120/gp41 cleavage. The cytoplasmic tail-truncated proteins were found to be incorporated into virions by forming an oligomer with ***wild*** -type TM, but could not inhibit the ***wild*** -type function. In contrast, phenotypic mixing of cleavage-defective Env with the ***wild*** -type protein caused dramatic inhibition of infectivity, indicating that this ***mutant*** has a strong ***dominant*** - ***negative*** phenotype. .COPYRGT. 2001 Academic Press.

L6 ANSWER 8 OF 31 EMBASE COPYRIGHT 2003 ELSEVIER INC. ALL RIGHTS RESERVED.
on STN
ACCESSION NUMBER: 2001006370 EMBASE
TITLE: Binding of BiP to the processing enzyme lymphoma proprotein convertase prevents aggregation, but slows down maturation.
AUTHOR: Creemers J.W.M.; Van de Loo J.-W.H.P.; Plets E.; Hendershot L.M.; Van de Ven W.J.M.
CORPORATE SOURCE: Dr. J.W.M. Creemers, Laboratory for Molecular Oncology, Center for Human Genetics, University of Leuven, Herestraat 49, 3000 Leuven, Belgium.
john.creemers@med.kuleuven.ac.be
SOURCE: Journal of Biological Chemistry, (8 Dec 2000) 275/49

(38842-38847).
Refs: 55
ISSN: 0021-9258 CODEN: JBCHA3
COUNTRY: United States
DOCUMENT TYPE: Journal; Article
FILE SEGMENT: 016 Cancer
029 Clinical Biochemistry
LANGUAGE: English
SUMMARY LANGUAGE: English
AB Lymphoma proprotein convertase (LPC) is a subtilisin-like serine protease of the mammalian proprotein convertase family. It is synthesized as an inactive precursor protein, and propeptide cleavage occurs via intramolecular cleavage in the endoplasmic reticulum. In contrast to other convertases like furin and proprotein convertase-1, propeptide cleavage occurs slowly. Also, both a glycosylated and an unglycosylated precursor are detected. Here we demonstrate that the unglycosylated precursor form of LPC is localized in the cytosol due to the absence of a signal peptide. Using a reducible cross-linker, we found that glycosylated pro-LPC is associated with the molecular chaperone BiP. In addition, we show that

pro-LPC is prone to aggregation and forms large complexes linked via interchain disulfide bonds. BiP is associated mainly with non-aggregated pro-LPC and pro-LPC dimers and ***trimers***, suggesting that BiP prevents aggregation. Overexpression of ***wild*** -type BiP or a ***dominant*** - ***negative*** BiP ATPase ***mutant*** resulted in reduced processing of pro-LPC. Taken together, these results suggest that binding of BiP to pro-LPC prevents aggregation, but results in slower maturation.

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on STN
ACCESSION NUMBER: 2000332799 EMBASE
TITLE: Reconstitution of the KRAB-KAP-1 repressor complex: A model system for defining the molecular anatomy of RING-B box-coiled-coil domain-mediated protein-protein interactions.
AUTHOR: Peng H.; Begg G.E.; Schultz D.C.; Friedman J.R.; Jensen D.E.; Speicher D.W.; Rauscher III F.J.
CORPORATE SOURCE: F.J. Rauscher III, Wistar Institute, 3601 Spruce Street, Philadelphia, PA 19104, United States.
rauscher@wista.wistar.upenn.edu
SOURCE: Journal of Molecular Biology, (4 Feb 2000) 295/5

(1139-1162).
Refs: 61
ISSN: 0022-2836 CODEN: JMOBAK
COUNTRY: United Kingdom
DOCUMENT TYPE: Journal; Article
FILE SEGMENT: 029 Clinical Biochemistry
LANGUAGE: English
SUMMARY LANGUAGE: English
AB The KRAB domain is a 75 amino acid residue transcriptional repression module commonly found in eukaryotic zinc-finger proteins. KRAB-mediated gene silencing requires binding to the corepressor KAP-1. The KRAB:KAP-1 interaction requires the RING-B box-coiled coil (RBCC) domain of KAP-1, which is a widely distributed motif, hypothesized to be a protein-protein interface. Little is known about RBCC-mediated ligand binding and the role of the individual sub-domains in recognition and specificity. We have addressed these issues by reconstituting and characterizing the KRAB:KAP-1-RBCC interaction using purified components. Our results show that KRAB binding to KAP-1 is direct and specific, as the related RBCC domains from TIF1.alpha. and MID1 do not bind the KRAB domain. A combination of gel filtration, analytical ultracentrifugation, chemical cross-linking, non-denaturing gel electrophoresis, and site-directed

mutagenesis techniques has revealed that the KAP-1-RBCC must oligomerize likely as a homo- ***trimer*** in order to bind the KRAB domain. The RING finger, B2 box, and coiled-coil region are required for oligomerization of KAP-1-RBCC and KRAB binding, as mutations in these domains concomitantly abolished these functions. KRAB domain binding stabilized the homo-oligomeric state of the KAP-1-RBCC as detected by chemical cross-linking and velocity sedimentation studies. ***Mutant*** KAP-1-RBCC molecules hetero-oligomerize with the ***wild*** -type KAP-1, but these complexes were inactive for KRAB binding, suggesting a potential ***dominant*** ***negative*** activity. Substitution of the coiled-coil region with heterologous dimerization, ***trimerization***, or tetramerization domains failed to recapitulate KRAB domain binding. Chimeric KAP-1-RBCC proteins containing either the RING, RING-B box, or coiled-coil regions from MID1 also failed to bind the KRAB domain. The KAP-1-RBCC mediates a highly specific, direct interaction with the KRAB domain, and it appears to function as an integrated, possibly cooperative structural unit wherein each sub-domain contributes to oligomerization and/or ligand recognition. These observations provide the first principles for RBCC domain-mediated protein-protein interaction and have implications for identifying new ligands for RBCC domain proteins. (C) 2000 Academic Press.

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on STN DUPLICATE 7
ACCESSION NUMBER: 1999245702 EMBASE
TITLE: Disruption of coiled-coil domains in Fer protein-tyrosine kinase abolishes trimerization but not kinase activation.
AUTHOR: Craig A.W.B.; Zirngibl R.; Greer P.
CORPORATE SOURCE: P. Greer, Cancer Research Labs, Botterell Hall, Queen's University, Kingston, Ont. K7L 3N6, Canada.
greerp@post.queensu.ca
SOURCE: Journal of Biological Chemistry, (9 Jul 1999) 274/28 (19934-19942).
Refs: 53
ISSN: 0021-9258 CODEN: JBCHA3
COUNTRY: United States
DOCUMENT TYPE: Journal; Article
FILE SEGMENT: 029 Clinical Biochemistry
LANGUAGE: English
SUMMARY LANGUAGE: English
AB The protein-tyrosine kinase Fer and the highly homologous proto-oncoprotein Fps/Fes are implicated in signaling from a variety of growth

factor and cytokine receptors. Here we examine the molecular basis of Fer kinase activation with an emphasis on the role of oligomerization. We show that Fer forms ***trimers*** in vivo and that disruption of either the first or second coiled-coil domain abolishes oligomerization, suggesting a cooperative interaction between these two domains. Although Fps/Fes also forms homotypic oligomers, probably via homologous coiled-coil domains, no heterotypic interactions were observed between Fer and Fps/Fes. Incorporation of catalytically inactive Fer peptides into the oligomeric complex caused only mild reduction of ***wild*** type Fer kinase activity, suggesting that kinase-inactive Fer would not behave as a potent ***dominant*** ***negative***. Although oligomerization of Fer can potentiate autophosphorylation in trans at three major phosphorylation sites, these residues can likely also be phosphorylated in cis. In contrast, the testis-specific FerT isomer does not oligomerize and is able to autophosphorylate in cis at two of the same three residues autophosphorylated in Fer. These results suggest that although oligomerization potentiates autophosphorylation in trans, this is apparently not necessary for Fer activation.

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on STN DUPLICATE 8
ACCESSION NUMBER: 1999111160 EMBASE
TITLE: Fas ligand-independent, FADD-mediated activation of the Fas death pathway by anticancer drugs.
AUTHOR: Micheau O.; Solary E.; Hammann A.; Dimanche-Boitrel M.-T.
CORPORATE SOURCE: M.-T. Dimanche-Boitrel, INSERM U517, Pole Biol./Therapie Cancers (JE 515), Faculty of Medicine and Pharmacy, 7 boulevard Jeanne d'Arc, 21033 Dijon Cedex, France.
mtboitre@u-bourgogne.fr
SOURCE: Journal of Biological Chemistry, (19 Mar 1999) 274/12 (7987-7992).
Refs: 31
ISSN: 0021-9258 CODEN: JBCHA3
COUNTRY: United States
DOCUMENT TYPE: Journal; Article
FILE SEGMENT: 016 Cancer
030 Pharmacology
037 Drug Literature Index
LANGUAGE: English
SUMMARY LANGUAGE: English
AB ***Trimerization*** of the Fas receptor (CD95, APO-1), a membrane bound protein, triggers cell death by apoptosis. The main death pathway activated by Fas receptor involves the adaptor protein FADD (for

Fas-associated death domain) that connects Fas receptor to the caspase cascade. Anticancer drugs have been shown to enhance both Fas receptor and Fas ligand expression on tumor cells. The contribution of Fas ligand-Fas receptor interactions to the cytotoxic activity of these drugs remains controversial. Here, we show that neither the antagonistic anti-Fas antibody ZB4 nor the Fas-IgG molecule inhibit drug-induced apoptosis in three different cell lines. The expression of Fas ligand on the plasma membrane, which is identified in untreated U937 human leukemic cells but remains undetectable in untreated HT29 and HCT116 human colon cancer cell lines, is not modified by exposure to various cytotoxic agents. These drugs induce the clustering of Fas receptor, as observed by confocal laser scanning microscopy, and its interaction with FADD, as demonstrated by co-immunoprecipitation. Overexpression of FADD by stable transfection sensitizes tumor cells to drug-induced cell death and cytotoxicity, whereas down-regulation of FADD by transient transfection of an antisense construct decreases tumor cell sensitivity to drug-induced apoptosis. These results were confirmed by transient transfection of constructs encoding either a FADD ***dominant*** ***negative*** or MC159 or E8 viral proteins that inhibit the FADD/caspase-8 pathway. These results suggest that drug-induced cell death involves the Fas/FADD pathway in a Fas ligand-independent fashion.

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on STN
 ACCESSION NUMBER: 1999189724 EMBASE
 TITLE: Down-regulation of cyclin B1 gene transcription in terminally differentiated skeletal muscle cells is associated with loss of functional CCAAT-binding NF-Y complex.

AUTHOR: Farina A.; Manni I.; Fontemaggi G.; Tiainen M.; Cenciarelli C.; Bellorini M.; Mantovani R.; Sacchi A.; Piaggio G.

CORPORATE SOURCE: G. Piaggio, Laboratorio di Oncogenesi Molecolare, (CRS-IRE), Via delle Messi D'Oro 156, 00158 Roma, Italy
 SOURCE: Oncogene, (6 May 1999) 18/18 (2818-2827).

Refs: 45
 ISSN: 0950-9232 CODEN: ONCNES
 COUNTRY: United Kingdom
 DOCUMENT TYPE: Journal; Article
 FILE SEGMENT: 029 Clinical Biochemistry
 LANGUAGE: English

SUMMARY LANGUAGE: English

AB The observation that cyclin B1 protein and mRNAs are down-regulated in terminally differentiated (TD) C2C12 cells, suggested us to investigate the transcriptional regulation of the cyclin B1 gene in these cells.

Transfections of cyclin B1 promoter constructs indicate that two CCAAT boxes support cyclin B1 promoter activity in proliferating cells. EMSAs demonstrate that both CCAAT boxes are recognized by the ***trimeric*** NF-Y complex in proliferating but not in TD cells.

Transfecting a ***dominant*** - ***negative*** ***mutant*** of NF-YA we provide evidence that NF-Y is required for maximal promoter activity. Addition of recombinant NF-YA to TD C2C12 nuclear extracts restores binding activity in vitro, thus indicating that the loss of NF-YA in TD cells is responsible for the lack of the NF-Y binding to the CCAAT boxes.

Consistent with this, we found that the NF-YA protein is absent in TD C2C12 cells. In conclusion, our data demonstrate that NF-Y is required for cyclin B1 promoter activity. We also demonstrate that cyclin B1 expression is regulated at the transcriptional level in TD C2C12 cells and that the switch-off of cyclin B1 promoter activity in differentiated cells depends upon the loss of a functional NF-Y complex. In particular the loss of NF-YA protein is most likely responsible for its inactivation.

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on STN
 ACCESSION NUMBER: 1999256690 EMBASE
 TITLE: Assembly of a novel cartilage matrix protein filamentous network: Molecular basis of differential requirement of von Willebrand factor A domains.

AUTHOR: Chen Q.; Zhang Y.; Johnson D.M.; Goetinck P.F.
 CORPORATE SOURCE: Q. Chen, Musculoskeletal Research Laboratory, Dept. of Orthopaedics/Rehabilitation, Pennsylvania State University, Hershey, PA 17033, United States.

qchen@ortho.hmc.psu.edu
 SOURCE: Molecular Biology of the Cell, (1999) 10/7 (2149-2162).

Refs: 34
 ISSN: 1059-1524 CODEN: MBCEEV

COUNTRY: United States
 DOCUMENT TYPE: Journal; Article
 FILE SEGMENT: 029 Clinical Biochemistry
 LANGUAGE: English
 SUMMARY LANGUAGE: English
 AB Cartilage matrix protein (CMP) is the prototype of the newly discovered matrilin family, all of which contain von Willebrand factor A domains.

Although the function of matrilins remain unclear, we have shown that, in primary chondrocyte cultures, CMP (matrilin-1) forms a filamentous network, which is made up of two types of filaments, a collagen-dependent one and a collagen-independent one. In this study, we demonstrate that the collagen-independent CMP filaments are enriched in pericellular compartments, extending directly from chondrocyte membranes. Their morphology can be distinguished from that of collagen filaments by immunogold electron microscopy, and mimicked by that of self-assembled purified CMP. The assembly of CMP filaments can occur from transfection of a ***wild*** -type CMP transgene alone in skin fibroblasts, which do not produce endogenous CMP. Conversely, assembly of endogenous CMP filaments by chondrocytes can be inhibited specifically by ***dominant*** ***negative*** CMP transgenes. The two A domains within CMP serve essential but different functions during network formation. Deletion of the A2 domain converts the ***trimeric*** CMP into a mixture of monomers, dimers, and ***trimers***, whereas deletion of the A1 domain does not affect the ***trimeric*** configuration. This suggests that the A2 domain modulates multimerization of CMP. Absence of either A domain from CMP abolishes its ability to form collagen-independent filaments. In particular, Asp22 in A1 and Asp255 in A2 are essential; double point mutation of these residues disrupts CMP network formation. These residues are part of the metal ion-dependent adhesion sites, thus a metal ion-dependent adhesion site-mediated adhesion mechanism may be applicable to matrilin assembly. Taken together, our data suggest that CMP is a bridging molecule that connects matrix components in cartilage to form an integrated matrix network.

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on STN
 ACCESSION NUMBER: 1999112263 EMBASE
 TITLE: The cyclin B2 promoter depends on NF-Y, a trimer whose CCAAT-binding activity is cell-cycle regulated.
 AUTHOR: Bolognese F.; Wasner M.; Lange-zu Dohna C.; Gurtner A.; Ronchi A.; Muller H.; Manni I.; Mossner J.; Piaggio G.; Mantovani R.; Engeland K.
 CORPORATE SOURCE: R. Mantovani, Dipt. Gen. Biologia Microrganismo, Univesita di Milano, Via Celoria 26, 20133 Milano, Italy

SOURCE: Oncogene, (11 Mar 1999) 18/10 (1845-1853).

Refs: 52

ISSN: 0950-9232 CODEN: ONCNES

COUNTRY: United Kingdom
 DOCUMENT TYPE: Journal; Article
 FILE SEGMENT: 029 Clinical Biochemistry
 LANGUAGE: English
 SUMMARY LANGUAGE: English
 AB Cyclin B2 is a regulator of p34cdc2 kinase, involved in G2/M progression of the cell cycle, whose gene is strictly regulated at the transcriptional level in cycling cells. The mouse promoter was cloned and three conserved CCAAT boxes were found. In this study, we analysed the mechanisms leading to activation of the cyclin B2 CCAAT boxes: a combination of (i) genomic footprinting, (ii) transfections with single, double and triple ***mutants***, (iii) EMSAs with nuclear extracts, antibodies and NF-Y recombinant proteins and (iv) transfections with an NF-YA ***dominant*** ***negative*** ***mutant*** established the positive role of the three CCAAT sequences and proved that NF-Y plays a crucial role in their activation. NF-Y, an ubiquitous ***trimer*** containing histone fold subunits, activates several other promoters regulated during the cell cycle. To analyse the levels of NF-Y subunits in the different phases of the cycle we separated MEL cells by elutriation, obtaining fractions > 80% pure. The mRNA and protein levels of the histone-fold containing NF-YB and NF-YC were invariant, whereas the NF-YA protein, but not its mRNA, was maximal in mid-S and decreased in G2/M. EMSA confirmed that the CCAAT-binding activity followed the amount of NF-YA, indicating that this subunit is limiting within the NF-Y complex, and suggesting that post-transcriptional mechanisms regulate NF-YA levels. Our results support a model whereby fine tuning of this activator is important for phase-specific transcription of CCAAT-containing promoters.

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on STN
 ACCESSION NUMBER: 1999295218 EMBASE
 TITLE: Dominant negative mutations in the .alpha.-factor receptor, a G protein-coupled receptor encoded by the STE2 gene of the yeast Saccharomyces cerevisiae.
 AUTHOR: Leavitt L.M.; Macaluso C.R.; Kim K.S.; Martin N.P.; Dumont M.E.
 CORPORATE SOURCE: M.E. Dumont, Department Biochemistry Biophysics, University Rochester Medical Center, 575 Elmwood Avenue, Rochester, NY

14642, United States
 SOURCE: Molecular and General Genetics,
 (1999) 261/6 (917-932).
 Refs: 65
 ISSN: 0026-8925 CODEN: MGGEAE
 COUNTRY: Germany
 DOCUMENT TYPE: Journal; Article
 FILE SEGMENT: 004 Microbiology
 022 Human Genetics
 LANGUAGE: English
 SUMMARY LANGUAGE: English
 AB The .alpha.-mating pheromone receptor encoded
 by the STE2 gene of the
 yeast *Saccharomyces cerevisiae* is a G protein-
 coupled receptor (GPCR) that
 is homologous to the large family of GPCRs that
 mediate multiple types of
 signal transduction in mammals. We have screened
 libraries of
 mutant receptors to identify ***dominant***
 negative
 alleles that are capable of interfering with the
 function of a
 co-expressed normal receptor. Two ***dominant***
 negative
 alleles have been recovered in this manner. In
 addition, we find that
 previously isolated loss-of-function mutations in the
 .alpha.-factor
 receptor exhibit ***dominant*** ***negative***
 effects. Detection
 of the dominant effects requires high-level
 expression of the
 mutant receptors but does not require a high
 ratio of
 mutant to normal receptors. Cellular levels of
 the normal
 receptors are not affected by co-expression of the
 dominant
 negative alleles. Expression of the
 mutant receptors
 does not interfere with constitutive signaling in a
 strain that lacks the
 G protein .alpha. subunit encoded by GPA1,
 indicating that interference
 with signaling occurs at the level of the receptor or
 the interacting G
 protein. Expression of increased levels of G protein
 subunits partially
 reverses the ***dominant*** ***negative***
 effects. The
 dominant ***negative*** behavior of the
 mutant
 receptors is diminished by deletion of the SST2
 gene, which encodes an RGS
 (Regulator of G protein Signaling) protein involved in
 desensitization of
 pheromone signaling. The most likely explanation for
 the ***dominant***
 negative effects of the mutations appears to
 be the existence of
 an interaction between unactivated receptors and
 the ***trimeric*** G
 protein that titrates the G protein away from the
 normal receptors or
 renders the G protein insensitive to receptor
 activation. This interaction
 appears to be mediated by the SST2 gene product.

L6 ANSWER 16 OF 31 EMBASE COPYRIGHT 2003
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 on STN
 ACCESSION NUMBER: 1999046957 EMBASE
 TITLE: A G(s.alpha.) mutant designed to inhibit
 receptor signaling
 through G(s).
 AUTHOR: Iiri T.; Bell S.M.; Baranski T.J.; Fujita
 T.; Bourne H.R.
 CORPORATE SOURCE: H.R. Bourne, Box 0450,
 Univ. of California Medical Center,
 San Francisco, CA 94143, United States
 SOURCE: Proceedings of the National
 Academy of Sciences of the
 United States of America, (19 Jan 1999)
 96/2 (499-504).
 Refs: 42
 ISSN: 0027-8424 CODEN: PNASA6
 COUNTRY: United States
 DOCUMENT TYPE: Journal; Article
 FILE SEGMENT: 022 Human Genetics
 029 Clinical Biochemistry
 LANGUAGE: English
 SUMMARY LANGUAGE: English
 AB Hormonal signals activate ***trimeric*** G
 proteins by substituting
 GTP for GDP bound to the G protein .alpha. subunit
 (G.alpha.), thereby
 generating two potential signaling molecules,
 G.alpha.-GTP and free
 G.beta..gamma.. The usefulness of ***dominant***
 negative
 mutations for investigating Ras and other
 monomeric G proteins inspired us
 to create a functionally analogous ***dominant***
 negative
 G.alpha. mutation. Here we describe a ***mutant***
 .alpha. subunit
 designed to inhibit receptor- mediated hormonal
 activation of G(s), the
 stimulatory regulator of adenylyl cyclase. To
 construct this
 mutant, we introduced into the .alpha.
 subunit (fs) of G(s) three
 separate mutations chosen because they impair as
 function in complementary
 ways: the A366S ***mutant*** reduces affinity of
 as for binding GDP,
 whereas the G226A and E268A mutations impair the
 protein's ability to bind
 GTP and to assume an active conformation. The
 triple ***mutant***
 robustly inhibits (by up to 80%) G(s)-dependent
 hormonal stimulation of
 adenylyl cyclase in cultured cells. Inhibition is
 selective in that it
 does not affect cellular responses to expression of a
 constitutively
 active (s) ***mutant*** (.alpha.(s)-R201C) or to
 agonists for
 receptors that activate G(q) or Gi. This .alpha.(s)
 triple ***mutant***
 and cognate G.alpha. ***mutants*** should
 provide specific tools for
 dissection of G protein-mediated signals in cultured
 cells and transgenic
 animals.

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on STN
 ACCESSION NUMBER: 1998137970 EMBASE
 TITLE: Effect of cleavage mutants on
 syncytium formation directed
 by the wild- type fusion protein of
 newcastle disease
 virus.
 AUTHOR: Li Z.; Serpel T.; Razvi E.; Morrison T.
 CORPORATE SOURCE: T. Morrison, Dept. of Molec.
 Genetics/Microbiol., Univ. of
 Massachusetts Med. School, 55 Lake Ave.
 North, Worcester,
 MA 01655, United States.
 trudy.morrison@banyan.ummed.edu
 SOURCE: Journal of Virology, (1998) 72/5
 (3789-3795).

Refs: 29
 ISSN: 0022-538X CODEN: JOVIAM
 COUNTRY: United States
 DOCUMENT TYPE: Journal; Article
 FILE SEGMENT: 004 Microbiology
 LANGUAGE: English
 SUMMARY LANGUAGE: English
 AB The effects of Newcastle disease virus (NDV)
 fusion (F) glycoprotein
 cleavage ***mutants*** on the cleavage and
 syncytium-forming activity
 of the ***wild*** - type F protein were examined. F
 protein cleavage
 mutants were made by altering amino acids
 in the furin recognition
 region (amino acids 112 to 116) in the F protein of a
 virulent strain of
 NDV. Four ***mutants*** were made: Q114P
 replaced the glutamine
 residue with proline; K115G replaced lysine with
 glycine; double
 mutant K115G, R113G replaced both a
 lysine and an arginine with
 glycine residues; and a triple ***mutant*** ,
 R112G, K115G, F117L,
 replaced three amino acids to mimic the sequence
 found in avirulent
 strains of NDV. All ***mutants*** except Q114P
 were cleavage negative
 and fusion negative. However, addition of
 exogenous trypsin cleaved all
 mutant F proteins and activated fusion. As
 expected for an
 oligomeric protein, the fusion-negative
 mutants had a
 dominant ***negative*** phenotype:
 cotransfection of
 wild -type and ***mutant*** F protein
 cDNAs resulted in an
 inhibition of syncytium formation. The presence of
 the ***mutant*** F
 protein did not inhibit cleavage of the ***wild*** -
 type protein.
 Furthermore, evidence is presented that suggests
 that the ***mutant***
 protein and the ***wild*** -type protein formed
 heterooligomers. By
 measuring the syncytium-forming activity of the
 wild -type
 protein at various ratios of expression of
 mutant and
 wild -type protein, results were obtained that
 are most consistent

with the notion that the size of the functionally active
 NDV F protein in
 these assays is a single oligomer, likely a
 trimer. That a
 larger oligomer, containing a mix of both ***wild***
 -type and
 mutant F proteins, has partial activity cannot,
 however, be ruled
 out.

L6 ANSWER 18 OF 31 EMBASE COPYRIGHT 2003
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 on STN DUPLICATE 9
 ACCESSION NUMBER: 1998114791 EMBASE
 TITLE: A naturally occurring isoform of the
 human macrophage
 scavenger receptor (SR-A) gene generated
 by alternative
 splicing blocks modified LDL uptake.
 AUTHOR: Gough P.J.; Greaves D.R.; Gordon
 S.
 CORPORATE SOURCE: P.J. Gough, Sir William
 Dunn School of Pathology,
 University of Oxford, South Parks Road,
 Oxford OX1 3RE,
 United Kingdom
 SOURCE: Journal of Lipid Research, (1998)
 39/3 (531-543).

Refs: 36
 ISSN: 0022-2275 CODEN: JLPRAW
 COUNTRY: United States
 DOCUMENT TYPE: Journal; Article
 FILE SEGMENT: 018 Cardiovascular Diseases
 and Cardiovascular Surgery
 029 Clinical Biochemistry
 LANGUAGE: English
 SUMMARY LANGUAGE: English
 AB The class A macrophage scavenger receptors
 (SPA) are macrophage-specific
 trimeric integral membrane glycoproteins
 that have been implicated
 in many macrophage-associated physiological and
 pathological processes
 including atherosclerosis, Alzheimer's disease, and
 host defense. There
 are two forms of the receptor that have been
 previously cloned, and both
 are generated by alternative splicing of a single
 gene. Here we report the
 cloning of a third, alternatively spliced isoform of the
 human SR-A gene
 (type III hSRA). The novel isoform is expressed in
 the human monocytic
 leukemia cell line THP-1 and also in primary human
 monocyte derived
 macrophages. When expressed in CHO-K1 cells,
 type III hSR-A does not
 internalize AcLDL despite having the domain shown
 to mediate this function
 in type I and II hSR-A. We show that type III protein
 has altered
 intracellular processing and is trapped within the
 endoplasmic reticulum,
 making it unable to perform endocytosis. Type III
 protein acts as a
 dominant ***negative*** isoform by
 reducing modified LDL
 uptake in CHO cells stably expressing either type I
 or type II SR-A. The

demonstration that a naturally occurring splice
 variant of SR-A
 mRNA can act as a ***dominant***
 negative isoform suggests a
 novel mechanism for regulation of scavenger
 receptor activity in
 macrophages.

L6 ANSWER 19 OF 31 EMBASE COPYRIGHT 2003
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on STN
 ACCESSION NUMBER: 1998316914 EMBASE
 TITLE: Possible existence of quaternary
 structure in the
 high-affinity serotonin transport complex.

AUTHOR: Chang A.S.; Starnes D.M.; Chang
 S.M.
 CORPORATE SOURCE: Dr. A.S. Chang, CWRU
 School of Medicine, 17815 Lakewood
 Heights Boulevard, Lakewood, OH 44107,
 United States.

asc6@po.cwru.edu
 SOURCE: Biochemical and Biophysical
 Research Communications, (19
 Aug 1998) 249/2 (416-421).

Refs: 32
 ISSN: 0006-291X CODEN: BBRCA

COUNTRY: United States
 DOCUMENT TYPE: Journal; Article
 FILE SEGMENT: 008 Neurology and
 Neurosurgery

029 Clinical Biochemistry

LANGUAGE: English

SUMMARY LANGUAGE: English

AB Deletion- ***mutants*** of the cloned mouse
 serotonin transporter
 (SERT) rendered ***dominant*** ***negative*** -
 mutant

effects upon ***wild*** -type transporter activities
 in heterologous

expression studies; such effects were transporter-
 selective and did not

influence the activities of co-expressed neuronal
 GABA transporter.

Heterologous expression of linear concatenates (up
 to four copies) of SERT

further revealed discernable uptake activities for
 both transporter-dimer

and -tetramer, but not for the ***trimer***. Kinetic
 and

pharmacological analyses revealed that the
 monomer, dimer, and tetramer

manifested comparable transport K(m) and

potencies for known serotonin

uptake inhibitors; the tetramer was distinct from the
 others only in

manifesting notably reduced transport V(max).

Surprisingly, equivalent

cocaine congener-binding activities were observed
 for all concatenates,

including the functionally inactive ***trimer***.

These findings

collectively support the existence of quaternary
 structure in the active

5-HT transport complex; such structure is likely to be
 a critical

determinant of ligand transport activities, but

apparently not of

transporter-inhibitor interactions.

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on STN
 ACCESSION NUMBER: 97192665 EMBASE
 DOCUMENT NUMBER: 1997192665
 TITLE: An evaluation of strategies available for
 the

identification of GTP-binding proteins
 required in

intracellular signalling pathways.

AUTHOR: Barritt G.J.; Gregory R.B.
 CORPORATE SOURCE: G.J. Barritt, Department of
 Medical Biochemistry, School of
 Medicine, Flinders University, GPO Box
 2100, Adelaide, SA

5001, Australia
 SOURCE: Cellular Signalling, (1997) 9/3-4
 (207-218).

Refs: 115
 ISSN: 0898-6568 CODEN: CESIEY
 PUBLISHER IDENT.: S 0898-6568(96)00131-3
 COUNTRY: United States
 DOCUMENT TYPE: Journal; General Review
 FILE SEGMENT: 029 Clinical Biochemistry
 LANGUAGE: English
 SUMMARY LANGUAGE: English
 AB Strategies which can be used to elucidate the
 nature of a GTP-binding
 regulatory protein (G-protein) involved in an
 intracellular pathway of
 interest in the complex environment of the cell are
 described and
 evaluated. A desirable strategy is considered to be
 one in which the first
 stage indicates a requirement for one or more G-
 proteins, provides
 information on whether a monomeric, ***trimeric***
 or other type of

G-protein is involved, and gives some idea of the G
 protein sub-class. In

the second stage the specific G-protein involved is
 identified. Approaches

available for investigations in the first stage include
 the use of

analogues of GTP and GDP, AIF4-, inhibitors of G-
 protein isoprenylation,

bacterial toxins which covalently modify G-proteins,
 and the introduction

of a purified GDP dissociation inhibitor, GDP
 exchange and/or GTP-ase

activating protein. Identification of the specific G-
 protein in the second

stage can be achieved using anti G-protein

antibodies, G-protein- or
 receptor-derived peptides, antisense G protein RNA

and over-expressed,
 constitutively-active or ***dominant*** -

negative G-protein

mutants. The correct interpretation of results
 obtained with GTP

and GDP analogues and AIF4- in the first stage is
 complex and often

difficult, and requires a thorough understanding of
 the functions and

mechanisms of activation of G-proteins.

Nevertheless, it is important to

reach the correct conclusion at this stage since

considerable time and

expense are usually required for investigations in the
 second stage.

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on STN

ACCESSION NUMBER: 97334294 EMBASE

DOCUMENT NUMBER: 1997334294

TITLE: Deletion mutants of the herpes simplex
virus type 1 UL8

protein: Effect on DNA synthesis and ability
to interact

with an influence the intracellular

localization of the UL5

and UL52 proteins.

AUTHOR: Barnard E.C.; Brown G.; Stow N.D.

CORPORATE SOURCE: N.D. Stow, MRC Virology

Unit, Institute of Virology, Church

Street, Glasgow G11 5JR, United

Kingdom.

n.stow@vir.gla.ac.uk

SOURCE: Virology, (1997) 237/1 (97-106).

Refs: 42

ISSN: 0042-6822 CODEN: VIRLAX

COUNTRY: United States

DOCUMENT TYPE: Journal; Article

FILE SEGMENT: 004 Microbiology

LANGUAGE: English

SUMMARY LANGUAGE: English

AB The herpes simplex virus type 1 (HSV-1) helicase-
primase, an essential

component of the viral DNA replication machinery, is
a ***trimeric***

complex of the virus-coded UL5, UL8, and UL52
proteins. An assembly of the

UL5 and UL52 subunits retains both enzymic
activities, and the UL3 protein

has been implicated in modulating these functions,
facilitating efficient

nuclear uptake of the complex and interacting with
other viral DNA

replication proteins. To further our understanding of
UL8, we have

constructed plasmids expressing ***mutant***
proteins, truncated at

their N- or C-termini or lacking amino acids

internally, under the control

of the human cytomegalovirus major immediate-
early promoter. Deletion of

23 amino acids from the N-terminus or 33 from the
C-terminus abolished the

ability of UL8 to support DNA replication in transient
transfection

assays. None of the UL8 ***mutants*** tested
exhibited a strong

dominant ***negative*** phenotype in the
presence of the

wild -type product, although some inhibition
of replication was

observed with ***mutants*** lacking 165 N-
terminal or 497 C-terminal

amino acids. The ability of the UL8 ***mutants***
to facilitate

efficient nuclear localization of UL52 in the presence
of coexpressed UL5

was examined by immunofluorescence. Selected
mutants were also

expressed by recombinant baculoviruses and tested
for interaction with UL5

and UL52 in immunoprecipitation assays. The
replicative ability of the

mutants was found to correlate with their
ability to localize UL52

to the nucleus, but not their interaction with UL5 and
UL52. This property

precluded the identification of any region of UL8
important for its

presumed nuclear functions.

L6 ANSWER 22 OF 31 CAPLUS COPYRIGHT 2003
ACS on STN

ACCESSION NUMBER: 1997:301161 CAPLUS

DOCUMENT NUMBER: 126:342347

TITLE: Functional and mutational analysis of

Fas receptor

(CD95) in three patients with

autoimmune

lymphoproliferative syndrome

AUTHOR(S): Wada, Taizo

CORPORATE SOURCE: Department Pediatrics,

School Medicine, Faculty

Medicine, Kanazawa University,

Kanazawa, 920, Japan

SOURCE: Kanazawa Daigaku Juzen Igakkai
Zasshi (1996), 105(6),

776-787

CODEN: JUZIAG; ISSN: 0022-7226

PUBLISHER: Juzen Igakkai

DOCUMENT TYPE: Journal

LANGUAGE: Japanese

AB The Fas receptor/Fas ligand system induces
apoptosis of Fas-bearing cells

and plays an important role in the immune

regulations, esp. in the

deletion of self-reactive clones. It is known that lpr
mice caused by the

Fas deficiency exhibit autoimmunity with abnormal
proliferation of

CD4-CD8- (double-neg.) T cells. Autoimmune
lymphoproliferative syndrome

(ALPS) was recently identified as a human
counterpart of the lpr mouse.

In this study, 3 cases of ALPS from two independent
families were

evaluated for immunol. and genetic abnormalities of
the Fas receptor.

They all exhibited lymphadenopathy,

hepatosplenomegaly, thrombocytopenia,

hypergammaglobulinemia and the increased no. of
double-neg. T cells from

early childhood. In patients 1 and 2 (family 1) who
were heterozygous in

the Fas receptor gene, the genomic sequence of the
mutant allele inherited

from their mother showed a T to C point mutation in
the 5' splice site of

intron 7, resulting in aberrant splicing. In the mutant
mRNA, 4 bases

insertion (GCAG) between exon 7 and 8 was

predicted to cause a frameshift

and premature termination after 9 missense codons.

The surface Fas

expression on activated T cells from these patients
was comparable to that

on normal T cells, but the truncated ***mutant***
proteins lacking the

death domain probably induced a ***dominant***
neg effect,

leading to the formation of abnormal ***trimers***
unable to transduce

the intracytoplasmic death signal. Although their mother had an identical mutation of the Fas receptor and exhibited a similar resistance to

Fas-mediated apoptosis at the cellular level, she remained asymptomatic.

These facts suggested that there exists an addnl. factor responsible for the manifestation of typical ALPS. Patient 3 (family 2) was born to parents who were cousins, and the genomic sequence of the homozygous mutant alleles showed an A to G point mutation in the 3' splice site of

the intron 3. The mRNA lacking exon 4 was predicted to have a frameshift and premature termination after 38 missense codons. Absence of the Fas expression may preclude any Fas-mediated signals and result in much

severer clin. features in this case. In all cases, activation-induced cell death of T cells was markedly diminished and Fas-induced apoptosis was defective. It was strongly suggested that these abnormalities of the

T cell function led to the failure in the exclusion of self-reactive T cell clones, resulting in the development of various autoimmune disorders.

Moreover, decreased Fas-mediated apoptosis of cultured B cells from these patients suggested that defective killing of the self-reactive B cells was directly related to the hypergammaglobulinemia and the autoantibody prodn.

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on STN

ACCESSION NUMBER: 96025328 EMBASE

DOCUMENT NUMBER: 1996025328

TITLE: PTP1D is a positive regulator of the prolactin signal

leading to .beta.-casein promoter activation.

AUTHOR: Ali S.; Chen Z.; Lebrun J.-J.; Vogel W.; Kharitonov A.;

Kelly P.A.; Ullrich A.

CORPORATE SOURCE: Department of Molecular Biology, Max-Planck-Institut für

Biochemie, Am Klopferspitz 18A, 82152 Martinsried, Germany

SOURCE: EMBO Journal, (1996) 15/1 (135-142).

ISSN: 0261-4189 CODEN: EMJODG

COUNTRY: United Kingdom

DOCUMENT TYPE: Journal; Article

FILE SEGMENT: 021 Developmental Biology and Teratology

029 Clinical Biochemistry

LANGUAGE: English

SUMMARY LANGUAGE: English

AB Stimulation of the prolactin receptor (PRLR), a member of the

cytokine/growth hormone receptor family, results in activation of the

associated Jak2 tyrosine kinase and downstream signaling pathways. We

report that PTP1D, a cytoplasmic protein tyrosine phosphatase containing

two Src homology 2 (SH2) domains, physically associates with the PRLR-Jak2

complex and is tyrosine-phosphorylated upon stimulation with prolactin.

The formation of the ***trimeric*** PRLR-Jak2-PTP1D complex is

critical for transmission of a lactogenic signal, while PTP1D

phosphorylation is necessary, but not sufficient. The ***dominant***

negative inhibitory effect of a phosphatase-deficient

mutant on expression of a .beta.-casein promoter-controlled

reporter gene is evidence for an essential role of fully functional PTP1D

in the regulation of milk protein gene transcription.

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on STN DUPLICATE 10

ACCESSION NUMBER: 96001797 EMBASE

DOCUMENT NUMBER: 1996001797

TITLE: Dominant-negative mutants of Grb2 induced reversal of the

transformed phenotypes caused by the point

mutation-activated rat HER-2/neu.

AUTHOR: Xie Y.; Pendergast A.M.; Hung M.-C.

CORPORATE SOURCE: Department of Tumor

Biology, Texas Univ. M. D. Anderson

Can. Ctr., Houston, TX 77030, United

States

SOURCE: Journal of Biological Chemistry, (1995) 270/51

(30717-30724).

ISSN: 0021-9258 CODEN: JBCHA3

COUNTRY: United States

DOCUMENT TYPE: Journal; Article

FILE SEGMENT: 029 Clinical Biochemistry

LANGUAGE: English

SUMMARY LANGUAGE: English

AB To clarify the role of the Shc-Grb2-Sos

trimer in the oncogenic

signaling of the point mutation-activated HER-2/neu receptor tyrosine

kinase (named p185), we interfered with the protein-protein interactions

in the Shc-Grb2-Sos complex by introducing Grb2

mutants with

deletions in either amino- (.DELTA.N- Grb2) or carboxyl(.delta.C-Grb2)

terminal SH3 domains into B104-1-1 cells derived from NIH3T3 cells

expressing the point mutation-activated HER-2/neu. We found that the

transformed phenotypes of the B104-1-1 cells were largely reversed by the

.DELTA.N-Grb2. The effect of the .DELTA.C-Grb2 was much weaker.

Biochemical analysis showed that the AN-Grb2 was able to associate Shc but

not p185 or Sos, while the .DELTA.C-Grb2 bound to Shc, p185, and Sos. The

p185-mediated Ras activation was severely inhibited by the .DELTA.N-Grb2

but not the .DELTA.C-Grb2. Taken together, these data demonstrate that

interruption of the interaction between Shc and the endogenous Grb2 by the .DELTA.N-Grb2 impairs the oncogenic signaling of the activated p185,

indicating that (i) the .DELTA.N-Grb2 functions as a strong

dominant - ***negative*** ***mutant*** , and (ii)

Shc/Grb2/Sos pathway plays a major role in mediating the oncogenic signal of the activated p185. Unlike the AN-Grb2, .DELTA.C-Grb2 appears to be a relatively weak ***dominant*** - ***negative*** ***mutant*** , probably due to its ability to largely fulfill the biological functions of the ***wild*** - type Grb2.

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on STN

ACCESSION NUMBER: 95290825 EMBASE

DOCUMENT NUMBER: 1995290825

TITLE: Purification and characterization of the G203T mutant

.alpha.(i-2) subunit of GTP-binding protein expressed in

baculovirus-infected sf9 cells.

AUTHOR: Inoue S.-I.; Hoshino S.-I.; Kukimoto I.; Ui M.; Katada T.

CORPORATE SOURCE: Dept. Physiological Chemistry, Faculty of Pharmaceutical Sciences, The University of Tokyo,Hongo, Bunkyo-ku, Tokyo 113, Japan

SOURCE: Journal of Biochemistry, (1995) 118/3 (650-657).

ISSN: 0021-924X CODEN: JOBIAO

COUNTRY: Japan

DOCUMENT TYPE: Journal; Article

FILE SEGMENT: 029 Clinical Biochemistry .

LANGUAGE: English

SUMMARY LANGUAGE: English

AB We expressed the Gly203.fwdarw.Thr (G203T)

mutant of

G(i2).alpha., which was expected to show a

dominant -

negative phenotype in G(i2)-mediated signal transduction, in

baculovirus-infected Sf9 cells and purified the

mutant at

subunit for its characterization. The rate of

dissociation of GDP from

G203T G(i2).alpha. was 3- to 4-fold faster than that from ***wild***

-type G(i2).alpha. but their k(cat) values for GTP hydrolysis were almost

the same. The affinities of the two G(i2).alpha. proteins for the

.beta..gamma. subunits of G proteins to form .alpha..beta..gamma.

trimers , which served as substrates for pertussis toxin-catalyzed

ADP-ribosylation, were the same. In marked contrast, G203T G(i2).alpha.

was unable to form a tight complex with a non-hydrolyzable analog

(GTP[.gamma.S]) of GTP; bound GTP[.gamma.S] was readily released from the

mutant G(i2).alpha. even in the presence of a high concentration

of Mg2+. Its susceptibility to tryptic digestion also revealed that

GTP[.gamma.S]-bound G203T G(i2).alpha. formed a conformation apparently

different from that of the GTP[.gamma.S]-bound form of ***wild*** -type

G(i2).alpha.. Both the G203T and ***wild*** -type G(i2).alpha. proteins

were capable of coupling with membrane-bound

.alpha.-adrenergic receptors,

resulting in the formation of receptor-.alpha. protein complexes with high

affinity for agonists. However, GTP[.gamma.S]-dependent uncoupling from

the high-affinity receptors was markedly attenuated in the case of G203T

G(i2).alpha.. Thus, G203T-mutated G(i2).alpha. had a unique property in

terms of coupling to membrane receptors, in addition to the previously

expected defect in the active conformation of the GTP-bound form of

G(i2).alpha..

L6 ANSWER 26 OF 31 MEDLINE on STN

DUPLICATE 11

ACCESSION NUMBER: 95268420 MEDLINE

DOCUMENT NUMBER: 95268420 PubMed ID: 7749409

TITLE: Concentration of mutations causing Schmid metaphyseal

chondrodysplasia in the C-terminal noncollagenous domain of

type X collagen.

AUTHOR: McIntosh I; Abbott M H; Francomano C A

CORPORATE SOURCE: Department of Medicine, Johns Hopkins University School of

Medicine, Baltimore, Maryland 21287,

USA.

SOURCE: HUMAN MUTATION, (1995) 5 (2) 121-5.

Journal code: 9215429. ISSN: 1059-7794.

PUB. COUNTRY: United States

DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)

LANGUAGE: English

FILE SEGMENT: Priority Journals

ENTRY MONTH: 199506

ENTRY DATE: Entered STN: 19950629

Last Updated on STN: 19950629

Entered Medline: 19950621

AB Schmid metaphyseal chondrodysplasia (SMCD)

has previously been shown to be

the result of mutations in the type X collagen gene, COL10A1. A further

three mutations have been identified, including two nonsense mutations

(Y268X, W651X) and a frameshift mutation

(1856delCC). Each of the 10 SMCD

mutations identified to date is within the C-terminal noncollagenous

domain of type X collagen and three of five deletions initiated around the

same nucleotide. This domain is believed to be involved in the initiation

of collagen trimerization. The concentration of mutations within this

domain is consistent with the hypothesis that the phenotype is the result of a reduction in the level of mature type X collagen due to the

mutant polypeptide's inability to participate in ***trimer*** formation, although a ***dominant*** - ***negative*** mechanism cannot be discounted, on the basis of current evidence.

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on STN DUPLICATE 12
ACCESSION NUMBER: 93206694 EMBASE
DOCUMENT NUMBER: 1993206694
TITLE: Characterization of an arginine 789 to cysteine

substitution in .alpha.1 (II) collagen chains of a patient

with spondyloepiphyseal dysplasia.
AUTHOR: Chan D.; Taylor T.K.F.; Cole W.G.
CORPORATE SOURCE: Division of Orthopaedics, Hospital for Sick Children, 555 University Ave., Toronto, Ont. M5G 1X8, Canada

SOURCE: Journal of Biological Chemistry, (1993) 268/20 (15238-15245).

ISSN: 0021-9258 CODEN: JBCHA3
COUNTRY: United States

DOCUMENT TYPE: Journal; Article
FILE SEGMENT: 007 Pediatrics and Pediatric Surgery

022 Human Genetics
029 Clinical Biochemistry

LANGUAGE: English

SUMMARY LANGUAGE: English

AB A child with spondyloepiphyseal dysplasia congenita was shown to be heterozygous for a mutation of the COL2A1 gene that encodes the .alpha.1(II) chain of type II collagen. The .alpha.1(II) chains extracted from cartilage contained disulfide-bonded dimeric and ***trimeric*** .alpha.1(II) chains. Carboxymethylation confirmed that some of the type II collagen chains contained cysteine residues that are not normally present in .alpha.1(II) chains. Cyanogen bromide peptide mapping showed that the abnormal cysteine residue was located in the .alpha.1(II) CB10.5 peptide.

Amplification products of the corresponding region of .alpha.1(II) cDNA

prepared from cultured dermal fibroblasts were shown by chemical cleavage and single strand conformation polymorphism analyses to contain a sequence anomaly. DNA sequencing showed a transition of C2913T in exon 41 of one allele of the COL2A1 gene resulting in the substitution of arginine 789 by cysteine in the .alpha.1(II) chain. The mutation resulted in the loss of a

Maell cleavage site that was used to confirm that the proband was heterozygous for the mutation and that neither parent showed evidence of

the mutation. The type II collagen extracted from cartilage and from chondrocytes cultured in alginate beads showed similar characteristics.

Approximately a third of the type II collagen chains were ***mutant***

, and the secretion of molecules containing ***mutant*** chains was impaired. The thermal stability of the collagen extracted from cartilage was normal. This study confirmed the importance of ***dominant***

negative mutations of the COL2A1 gene in producing the spondyloepiphyseal dysplasia congenita phenotype.

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on STN
ACCESSION NUMBER: 93070994 EMBASE
DOCUMENT NUMBER: 1993070994

TITLE: The collagenous domains of macrophage scavenger receptors and complement component C1q mediate their similar, but not

identical, binding specificities for polyanionic ligands.

AUTHOR: Acton S.; Resnick D.; Freeman M.; Ekkel Y.; Ashkenas J.; Krieger M.

CORPORATE SOURCE: Biology Department, Massachusetts Technology Institute, Cambridge, MA 02139, United States

SOURCE: Journal of Biological Chemistry, (1993) 268/5 (3530-3537).

ISSN: 0021-9258 CODEN: JBCHA3

COUNTRY: United States

DOCUMENT TYPE: Journal; Article

FILE SEGMENT: 029 Clinical Biochemistry

LANGUAGE: English

SUMMARY LANGUAGE: English

AB Macrophage scavenger receptors have been implicated in the development of atherosclerosis and other macrophage-associated functions, including host

defense. The mechanism by which these receptors bind a wide array of

polyanions, such as acetylated low density lipoprotein (Ac-LDL), with high affinity has not yet been elucidated; however, it has been proposed that

the positively charged extracellular collagenous domain of scavenger

receptors plays a key role in ligand binding. To test this proposal, we

generated truncation ***mutants*** of the bovine and murine scavenger

receptors and studied their expression in transiently transfected COS

cells. These ***mutants*** contain only 8 (bovine) or 5 (murine) of

the 24 Gly-X-Y tripeptide repeats found in the collagenous domains of the full-length receptors. Immunochemical analyses established that the

truncation of the bovine scavenger receptor did not interfere significantly with its synthesis, ***trimerization*** ,

post-translational processing, intracellular transport, surface expression, or stability. However, unlike their full-length counterparts, the truncated bovine and murine receptors were unable to bind Ac-LDL. Thus, the collagenous domain was necessary for normal ligand binding. In addition, cotransfection of the expression vector for the truncated bovine scavenger receptor with that for the full-length receptor resulted in dramatically reduced activity of the full-length construct (***dominant*** ***negative*** effect). A ligand bead-binding assay was used to show that the isolated collagenous domain from a different protein, complement component C1q, could bind a wide variety of polyanions with a specificity which was similar, but not identical, to that of scavenger receptors. These results suggest that the collagenous domain of the scavenger receptor is both necessary and sufficient to determine the broad binding specificity that characterizes this unusual receptor. Scavenger receptors and C1q, along with the mannose-binding protein, conglutinin, and lung surfactant apoprotein A, help define a set of proteins which all contain short collagenous domains and which all appear to participate in host defense. Their short collagenous domains may contribute significantly to their host-defense functions.

L6 ANSWER 29 OF 31 MEDLINE on STN
 DUPLICATE 13
 ACCESSION NUMBER: 93054492 MEDLINE
 DOCUMENT NUMBER: 93054492 PubMed ID:
 1429567
 TITLE: Negative complementation in aspartate
 transcarbamylase.
 Analysis of hybrid enzyme molecules
 containing different
 arrangements of polypeptide chains from
 wild-type and
 inactive mutant catalytic subunits.
 AUTHOR: Eisenstein E; Han M S; Woo T S;
 Ritchey J M; Gibbons I;
 Yang Y R; Schachman H K
 CORPORATE SOURCE: Department of Molecular
 and Cell Biology, University of
 California, Berkeley 94720.
 CONTRACT NUMBER: GM 11067 (NIGMS)
 GM 12159 (NIGMS)
 SOURCE: JOURNAL OF BIOLOGICAL
 CHEMISTRY, (1992 Nov 5) 267 (31)
 22148-55.
 Journal code: 2985121R. ISSN: 0021-
 9258.
 PUB. COUNTRY: United States
 DOCUMENT TYPE: Journal; Article; (JOURNAL
 ARTICLE)
 LANGUAGE: English
 FILE SEGMENT: Priority Journals
 ENTRY MONTH: 199212

ENTRY DATE: Entered STN: 19930122
 Last Updated on STN: 19970203
 Entered Medline: 19921201
 AB A comprehensive set of hybrid molecules of
 aspartate transcarbamylase
 (ATCase) from Escherichia coli has been
 constructed of wild-type and
 mutationally altered catalytic chains. The mutant
 enzymes that were
 virtually devoid of activity contained a replacement
 of Gly-128 in the
 catalytic polypeptide chains by either Asp or Arg.
 The kinetic properties
 of these hybrid enzyme-like molecules were
 analyzed to evaluate the basis
 for the unusual quaternary constraint demonstrated
 by an intersubunit
 hybrid containing one wild-type catalytic subunit, one
 inactive mutant
 subunit (containing the Gly to Asp replacement), and
 three wild-type
 regulatory subunits. A similar intersubunit hybrid
 was constructed from
 the wild-type catalytic subunit and the mutant in
 which Gly-128 was
 replaced by Arg, and it too demonstrated a
 pronounced decrease in activity
 relative to that expected for a hybrid containing three
 active sites.
 Moreover, neither of these hybrid holoenzymes
 exhibited the cooperativity
 with respect to aspartate that is characteristic of
 wild-type ATCase. In
 contrast, hybrid holoenzymes containing at least one
 wild-type chain in
 each catalytic subunit showed cooperativity. Also,
 hybrid enzymes
 containing different arrangements of five, four, three,
 or two wild-type
 catalytic chains with an appropriate complement of
 mutant chains had
 specific activities proportional to the number of wild-
 type chains in the
 holoenzymes. Exceptions were observed only in
 hybrids in which one of the
 two subunits in the holoenzyme was composed
 completely of mutant catalytic
 chains. For these hybrids the negative
 complementation was manifested as
 a much lower enzyme activity than expected from
 the number of wild-type
 chains in the enzyme and the loss of cooperativity.
 Thus, the activity
 and allosteric properties of these hybrids is
 dependent on the arrangement
 of catalytic chains in the holoenzyme, in contrast to
 results obtained for
 hybrids containing native and chemically modified
 catalytic chains.
 Intrасubunit hybrid catalytic ***trimers***
 containing one or two
 wild -type chains exhibited one-third and two-
 thirds the activity
 of the intact ***wild*** -type catalytic subunit,
 respectively,
 indicating the ***dominant*** ***negative***
 effect that was seen
 in intersubunit hybrid holoenzymes is absent within
 trimers :

L6 ANSWER 30 OF 31 EMBASE COPYRIGHT 2003
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on STN

ACCESSION NUMBER: 92354097 EMBASE

DOCUMENT NUMBER: 1992354097

TITLE: Human natriuretic peptide receptor-A
guanylyl cyclase is

self-associated prior to hormone binding.

AUTHOR: Lowe D.G.

CORPORATE SOURCE: Department of Molecular
Biology, Genentech, Inc., 460 Point

San Bruno Boulevard, South San

Francisco, CA 94080, United

States

SOURCE: Biochemistry, (1992) 31/43 (10421-
10425).

ISSN: 0006-2960 CODEN: BICHAW

COUNTRY: United States

DOCUMENT TYPE: Journal; Article

FILE SEGMENT: 003 Endocrinology

029 Clinical Biochemistry

LANGUAGE: English

SUMMARY LANGUAGE: English

AB The human natriuretic peptide receptor-A (NPR-A)
guanylyl cyclase is

specifically activated to synthesize cGMP by binding
of atrial natriuretic

peptide (ANP) to the receptor's extracellular domain.
In this report,

NPR-A monoclonal and polyclonal antibodies were
used to assess the

aggregation status of ***wild*** -type NPR-A and a
truncation

mutant lacking most of the NPR-A

cytoplasmic domain. On intact

human embryonic kidney 293 cells, in the absence
of ANP, recombinant human

NPR-A is self-aggregated through disulfide bonds in
an M(r) > 500 000,

possibly tetrameric, complex. Under nonreducing
conditions, truncated

NPR-A was a monomer, indicating that the

cytoplasmic domain is necessary

for NPR-A self-association. In the presence of the
homobifunctional

cross-linker dithiobis(succinimidyl propionate), or
disuccinimidyl suberate,

truncated NPR-A could be cross-linked as a dimer
and ***trimer*** only

in the presence of ANP. ***Wild*** -type NPR-A
was cross-linked with

disuccinimidyl suberate to an M(r) > 500 000

species in the absence of
ANP, and with ANP, a smaller, M(r) .simeq.400 000

receptor ***trimer***

cross-linking product was observed, together with
the larger, possibly

tetrameric complex. When whole cell stimulation of
cGMP production by ANP

was tested on the low level of endogenous 293 cell
NPR-A, maximal

stimulation was observed regardless of truncated
NPR-A overexpression. The

absence of a ***dominant*** ***negative***
effect by the truncated

NPR-A, together with the cross-linking data,
demonstrates that

preassociated NPR-A is the functionally relevant
form of this receptor.

L6 ANSWER,31 OF 31 MEDLINE on STN
DUPLICATE 14

ACCESSION NUMBER: 93046647 MEDLINE

DOCUMENT NUMBER: 93046647 PubMed ID:
1423608

TITLE: The reovirus cell attachment protein
possesses two

independently active trimerization domains:
basis of

dominant negative effects.

AUTHOR: Leone G; Maybaum L; Lee P W

CORPORATE SOURCE: Department of Microbiology
and Infectious Diseases,

University of Calgary Health Sciences

Center, Alberta,

Canada.

SOURCE: CELL, (1992 Oct 30) 71 (3) 479-88.

Journal code: 0413066. ISSN: 0092-8674.

PUB. COUNTRY: United States

DOCUMENT TYPE: Journal; Article; (JOURNAL
ARTICLE)

LANGUAGE: English

FILE SEGMENT: Priority Journals

ENTRY MONTH: 199212

ENTRY DATE: Entered STN: 19930122

Last Updated on STN: 20021019

Entered Medline: 19921208

AB The reovirus cell attachment protein, sigma 1, is a
homotrimer with an

N-terminal fibrous tail and a C-terminal globular
head. By cotranslating

full-length and various truncated sigma 1 proteins in
vitro, we show that

the N- and C-terminal halves of sigma 1 possess
independent trimerization

and folding domains. Trimerization of sigma 1 is
initiated at the

N-terminus by the formation of a "loose," protease-
sensitive,

three-stranded, alpha-helical coiled coil. This serves
to bring the three

unfolded C-termini into close proximity to one
another, facilitating their

subsequent trimerization and cooperative folding.

Concomitant with, but

independent of, this latter process, the N-terminal
fiber further matures

into a more stable and protease-resistant structure.
The coordinated

folding of sigma 1 ***trimers*** exemplifies the
dominant

negative effects of ***mutant*** subunits
in oligomeric

complexes.

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S2026		USPT	(dominant-negative or dominant adj negative) same ((mutant\$ or mutein\$ or variant\$ or wild\$)same (trimer\$))	<input type="checkbox"/>
S2025		USPT	(mutant\$ or mutein\$ or variant\$ or wild\$) same (trimer\$)	<input type="checkbox"/>
S2024		USPT	(mutant\$ or mutein\$ or variant\$ or wild\$) same (mutant\$ or mutein\$ or variant\$ or wild\$)	<input type="checkbox"/>
S2023		USPT	dominant-negative or dominant adj negative	<input type="checkbox"/>
S2022		USPT	trimer\$	<input type="checkbox"/>
S2021		USPT	mutant\$ or mutein\$ or variant\$ or wild\$	<input type="checkbox"/>
S2020		USPT	trimer?	<input type="checkbox"/>
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S2019		USPT	occurring))and (tnf or (tumor adj necrosis adj factor) or (tumour adj necrosis adj factor))and (trimer\$)) and ((wild or mutant\$ or mutein\$ or variant\$ or (non-naturally adj occurring))same (trimer\$))	<input type="checkbox"/>
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S2014		USPT	(wild or mutant\$ or mutein\$ or variant\$ or (non-naturally adj occurring)) and (tnf or (tumor adj necrosis adj factor) or (tumour adj necrosis adj factor)) and (trimer\$)	<input type="checkbox"/>
S2013		USPT	trimer\$	<input type="checkbox"/>

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S2008		USPT,PGPB,JPAB,EPAB,DWPI	trim\$	<input type="checkbox"/>
S2007		USPT,PGPB,JPAB,EPAB,DWPI	tnf or (tumor adj necrosis adj factor) or (tumour adj necrosis adj factor)	<input type="checkbox"/>
S2006		USPT,PGPB,JPAB,EPAB,DWPI	wild or mutant\$ or mutein\$ or variant\$ or (non-naturally adj occurring)	<input type="checkbox"/>
S2005		USPT,PGPB,JPAB,EPAB,DWPI	((trimer\$ or multimer\$)with (mix\$ or combination)) with (variant or mutant or mutein or (non-naturally adj occurring))	<input type="checkbox"/>
S2004		USPT,PGPB,JPAB,EPAB,DWPI	((trimer\$ or multimer\$)with (mix\$ or combination)) wit (variant or mutant or mutein or (non-naturally adj occurring))	<input type="checkbox"/>
S2003		USPT,PGPB,JPAB,EPAB,DWPI	(trimer\$ or multimer\$) with (mix\$ or combination)	<input type="checkbox"/>
S2002		USPT,PGPB,JPAB,EPAB,DWPI	mix\$ or combination	<input type="checkbox"/>

S2001	<input type="text"/>	USPT,PGPB,JPAB,EPAB,DWPI	((trimer\$ or multimer\$)with mix\$) same (variant or mutant or mutein or (non-naturally adj occurring))	<input type="checkbox"/>
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S1998	<input type="text"/>	USPT,PGPB,JPAB,EPAB,DWPI	(trimer\$ or multimer\$) with mix\$	<input type="checkbox"/>
S1997	<input type="text"/>	USPT,PGPB,JPAB,EPAB,DWPI	trimer\$ or multimer\$	<input type="checkbox"/>
S1996	<input type="text"/>	USPT,PGPB,JPAB,EPAB,DWPI	trimer\$ or multimer\$	<input type="checkbox"/>
S1995	<input type="text"/>	USPT	((variant or mutein or (non-naturally adj occurring))with (tNf or (tumor adj necrosis adj factor))) with trimer	<input type="checkbox"/>
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S1993	<input type="text"/>	USPT	((variant or mutein or (non-naturally adj occurring))same (tNf or (tumor adj necrosis adj factor))) and trimer	<input type="checkbox"/>
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